

107217
SEARCH REQUEST FORM RECEIVED

Scientific and Technical Information Center OCT 31 2003

Requester's Full Name: MOLLY CEPERLEY Examiner #: 59257 Date: 10/31/03
 Art Unit: 1641 Phone Number 303-4239 Serial Number: 10/025,378
 Mail Box and Bldg/Room Location: 8D15 Results Format Preferred (circle): PAPER DISK E-MAIL

7E12
 If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Tertiary Amine Compounds for use in Immunoassays

Inventors (please provide full names): Christopher C. Lawrence, Armen B. Shanafelt

Earliest Priority Filing Date: 12/18/01

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for particle agglutination assays which use a tertiary amine (formula (I) of claim 1) to avoid non-specific binding.

Prefer latex particles which have been activated by a carbodiimide (CDI).

Please also search the use of the tertiary amines listed in Table A of pages 18+19. (These may not fit the definitions of the tertiary amines in claim 1.).

Terms: latex agglutination, particle agglutination, ~~activated~~ carbodiimide activation, immunoassay, antibody, interference reduction, non-specific binding, unspecific binding.

Particle types: polystyrene, poly(methylmethacrylate) [PMMA], gold (nanoparticles and colloids), silica, glass, ceramics, alumina

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: _____	NA Sequence (#) _____	STN <u>711.99</u>
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) <u>1</u>	Questel/Orbit _____
Date Searcher Picked Up: <u>11/10</u>	Bibliographic _____	Dr. Link _____
Date Completed: <u>11/10</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: <u>30</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: <u>47</u>	Other _____	Other (specify) _____



STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact **the searcher or contact:**

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

➤ *I am an examiner in Workgroup:* *Example: 1610*

➤ *Relevant prior art found, search results used as follows:*

- 102 rejection
- 103 rejection
- Cited as being of interest.
- Helped examiner better understand the invention.
- Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- Foreign Patent(s)
- Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ *Relevant prior art not found:*

- Results verified the lack of relevant prior art (helped determine patentability).
- Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 - Circ. Desk



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Ak~O~Ak~G2
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O~Ak
@11 12

S~Ak
@13 14

O==C~O
15 @16 17

O==C~O~Ak
18 @19 20 21

O==C~N~Ak
22 @23 24 25

VAR G1=5/7

VAR G2=OH/11/13/16/19/23

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 2
CONNECT IS E2 RC AT 5
CONNECT IS E2 RC AT 7
CONNECT IS E2 RC AT 9
CONNECT IS E1 RC AT 12
CONNECT IS E2 RC AT 13
CONNECT IS E1 RC AT 14
CONNECT IS E1 RC AT 17
CONNECT IS E1 RC AT 21
CONNECT IS E2 RC AT 24
CONNECT IS E1 RC AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L6 405652 SEA FILE=REGISTRY ABB=ON PLU=ON (((N AND C AND O AND H)/ELS AND 4/ELC.SUB) OR ((N AND C AND S AND H)/ELS AND 4/ELC.SUB) OR ((N AND C AND O AND S AND H)/ELS AND 5/ELC.SUB)) AND NC=1 NOT RSD/FA
L11 651 SEA FILE=REGISTRY SUB=L6 SSS FUL L4
L14 1 SEA FILE=HCAPLUS ABB=ON PLU=ON 2003:488678/AN
L15 23324 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L16 23324 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 OR L15
L17 47217 SEA FILE=HCAPLUS ABB=ON PLU=ON IMMUNOASSAY+OLD,NT/CT
L18 55 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND L17
L19 707 SEA FILE=HCAPLUS ABB=ON PLU=ON CARBODIIMIDE/CT
L20 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 AND (L19 OR CARBODIIMID? OR CDI)
L21 6651 SEA FILE=HCAPLUS ABB=ON PLU=ON "AMINES (L) TERTIARY"/CT
L25 1317 SEA FILE=HCAPLUS ABB=ON PLU=ON "IMMUNOASSAY (L) AGGLUTINATION TEST"+OLD/CT
L26 5 SEA FILE=HCAPLUS ABB=ON PLU=ON (L16 OR L21) AND L25
L27 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 OR L26
L28 11 SEA FILE=HCAPLUS ABB=ON PLU=ON (L16 OR L21) AND (LATEX OR PARTICL?) (3A)AGGLUT?
L29 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 OR L28

*all considered
03/02/04
MEC*

=> ~~d 129 bibb abs hitind hitstr 1-12~~

L29 ANSWER 1 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2003:488678 HCPLUS
 DOCUMENT NUMBER: 139:49497
 TITLE: Tertiary amine compounds for use in immunoassays
 INVENTOR(S): Lawrence, Christopher C.; Shanafelt, Armen B.
 PATENT ASSIGNEE(S): Roche Diagnostics GmbH, Germany; F. Hoffmann-La Roche
 AG
 SOURCE: Eur. Pat. Appl., 13 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1321770	A2	20030625	EP 2002-27992	20021214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2003138974	A1	20030724	US 2001-25378	20011218
JP 2003207512	A2	20030725	JP 2002-363686	20021216
PRIORITY APPLN. INFO.: US 2001-25378 A 20011218				

OTHER SOURCE(S): MARPAT 139:49497

AB A reagent for use in immunoassays reduces interference in **particle agglutination** assays. The reagent contains particles having covalently bound antibodies and a tertiary amine compd. of formula (I): N(R1-X)(R2-Y)(R3-Z). The moieties R1, R2, and R3 are independently alkyl or alkyl ether. The moieties X, Y, and Z are independently -OH, -O-R4, -S-R4, -C(=O)-OH, -C(=O)-OR4, or -C(=O)-NHR4 and R4 is alkyl. Triethanolamine gave improved performance in **latex agglutination** immunoassays.

IC ICM G01N033-53
 ICS G01N033-543

CC 9-10 (Biochemical Methods)

ST tertiary amine reducing interference **particle agglutination** immunoassay; **latex agglutination** immunoassay triethanolamine reducing nonspecific binding

IT Immunoassay
 (agglutination test; tertiary amine compds. for reducing interference in **particle agglutination** immunoassays)

IT Antibodies
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (immobilized; tertiary amine compds. for reducing interference in **particle agglutination** immunoassays)

IT Immunoassay
 (latex agglutination test; tertiary amine compds. for reducing interference in **particle agglutination** immunoassays)

IT Antibodies
 RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses) (monoclonal, latex particles sensitized with; tertiary amine compds.)

for reducing interference in **particle agglutination immunoassays**)

IT **Carbodiimides**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (particle surface activation with; tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT **Latex**
 (particles; tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT **Amines, preparation**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (reaction products, with succinimide esters, on particle surface; tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT **Blood analysis**
Immobilization, molecular
Immunoassay
Microparticles
Test kits
 (tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT **Amines, analysis**
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (tertiary; tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT **Particles**
 (with immobilized antibodies; tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT 459-73-4DP, Glycine ethyl ester, reaction products with succinimide ester
 929-06-6DP, reaction products with succinimide ester 929-59-9DP,
 2,2'-(Ethylenedioxy)bisethylamine, reaction products with succinimide ester 4246-51-9DP, 4,7,10-Trioxa-1,13-tridecanediamine, reaction products with succinimide ester
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (on particle surface; tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

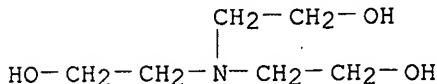
IT 1403-66-3, Gentamicin
 RL: ANT (Analyte); ANST (Analytical study)
 (tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT 102-71-6, Triethanolamine, analysis 104-78-9,
 3-Diethylaminopropylamine 109-54-6, Dimethylaminopropylchloride
 109-55-7, 3-Dimethylaminopropylamine 121-44-8, Triethylamine, analysis
 32897-26-0, 1-Ethyl-3-(3-dimethylaminopropyl)urea
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT 633-96-5 929-06-6 1892-57-5, 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide 6066-82-6, N-Hydroxysuccinimide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)

IT 123-56-8DP, Succinimide, esters, reaction products with primary amine on particle surface

RL: SPN (Synthetic preparation); PREP (Preparation)
 (tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)
 IT 102-71-6, Triethanolamine, analysis
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (tertiary amine compds. for reducing interference in **particle agglutination immunoassays**)
 RN 102-71-6 HCPLUS
 CN Ethanol, 2,2',2''-nitrilotris- (9CI) (CA INDEX NAME)



L29 ANSWER 2 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2003:355758 HCPLUS
 DOCUMENT NUMBER: 138:350816
 TITLE: Particles for immunoassays and methods for treating the same
 INVENTOR(S): Lawrence, Christopher C.; Yuan, Wei; Shanafelt, Armen B.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 53,058.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003087458	A1	20030508	US 2001-25196	20011218
US 2003092201	A1	20030515	US 2001-53058	20011102
EP 1319953	A1	20030618	EP 2002-24080	20021029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK JP 2003185667 A2 20030703 JP 2002-318893 20021031				
PRIORITY APPLN. INFO.:			US 2001-53058	A2 20011102
			US 2001-25196	A 20011218

OTHER SOURCE(S): MARPAT 138:350816
 AB A method of treating particles to be used in immunoassays reduces interference in **particle agglutination assays**. For particles having covalently bound antibodies and residual NHS-ester or sNHS-ester groups on the surface, the reactive esters are treated with an aq. mixt. contg. an amine compd. of formula (I): 2 The moiety -X is -NH₂, -OH, or -CO₂CH₂CH₃; and R is an alkyl group or an alkyl ether group. When -X is -NH₂ or -CO₂CH₂CH₃, R contains from 1 to 20 carbon atoms; and when -X is -OH, R contains from 4 to 20 carbon atoms.
 IC ICM G01N033-543
 ICS G01N033-545; B05D003-00
 NCL 436523000; 427002110
 CC 9-10 (Biochemical Methods)
 IT Immunoassay

(agglutination test, Particle;
 particles for immunoassays and methods for treating the same)

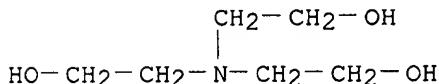
IT Adsorption
 Alkyl groups
 Amino group
 Blood serum
 Ceramics
 Chemical formula
 Coupling agents
 Hydroxyl group
Immunoassay
 Interference
 Latex
 Mixtures
 Particles
 Surface
 Test kits
 pH
 (particles for immunoassays and methods for treating the same)

IT **Carbodiimides**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (particles for immunoassays and methods for treating the same)

IT 79-09-4D, Propanoic acid, amines contg. 102-71-6,
 Triethanolamine, reactions 123-56-8D, Succinimide, esters 459-73-4,
 Glycine ethyl ester 929-06-6 929-59-9, 2,2'-
 (Ethylenedioxy)bisethylamine 4246-51-9, 4,7,10-Trioxa-1,13-
 tridecanediamine 6066-82-6, N-Hydroxysuccinimide 7440-44-0D, Carbon,
 amines contg. 7782-44-7D, Oxygen, compd. contg. 82436-78-0,
 N-Hydroxysulfosuccinimide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (particles for immunoassays and methods for treating the same)

IT 102-71-6, Triethanolamine, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (particles for immunoassays and methods for treating the same)

RN 102-71-6 HCPLUS
 CN Ethanol, 2,2',2'''-nitrilotris- (9CI) (CA INDEX NAME)



L29 ANSWER 3 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:31752 HCPLUS
 DOCUMENT NUMBER: 136:82290
 TITLE: Insoluble carrier particle nephelometric immunoassay
 reagent
 INVENTOR(S): Shigenobu, Kayoko; Oguri, Kazuhito
 PATENT ASSIGNEE(S): Kyowa Medex Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: *Patent*
 LANGUAGE: *Japanese*
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003068	A1	20020110	WO 2001-JP5115	20010615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001064293	A5	20020114	AU 2001-64293	20010615
EP 1298438	A1	20030402	EP 2001-938686	20010615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003143758	A1	20030731	US 2002-312328	20021226
PRIORITY APPLN. INFO.: JP 2000-198831 A 20000630 WO 2001-JP5115 W 20010615				

OTHER SOURCE(S): MARPAT 136:82290

AB An insol. carrier particle nephelometric immunoassay reagent or kit is provided, which produces an accurate measurement results due to the stabilized absorbance of a reaction liq. caused by stabilizing an agglutination reaction of insol. carrier particles such as latex by suppressing the function of a blood plasma component which participates in the agglutination reaction, and thereby, affects on the measurement values. An insol. carrier particle nephelometric immunoassay method using this reagent or kit is also provided. In this method, an antigen or antibody in a sample is quantitated by the processes of (1) immobilizing the antigen or antibody on the insol. carrier particles in the presence or absence of a buffer contg. a compd. possessing in the mol. the groups indicated in HOCH2CR2(R3)N(R1)CH2CO2H (I, R1, R2) and R3 may be the same or different from one another, and independently represent a H, a hydroxylalkyl group or the like; e.g., bicine, tricine); (2) performing an immuno-agglutination reaction by contacting a test sample with the antibody- or antigen-sensitized insol. carrier particle suspension in the presence of I; and (3) measuring the turbidity generated by the insol. carrier particle agglutination reaction.

IC ICM G01N033-543
ICS G01N033-58; G01N033-53

CC 9-10 (Biochemical Methods)

IT **Agglutination**

Blood plasma
Buffers
Carriers

Immobilization, molecular

Latex

Particles

Suspensions

Test kits

Turbidity

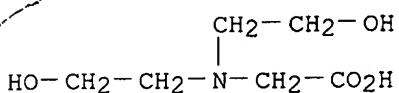
(insol. carrier particle nephelometric immunoassay reagent)

IT 150-25-4, Bicine 5704-04-1, Tricine
RL: ARU (Analytical role, unclassified); ANST (Analytical study)

(insol. carrier particle nephelometric immunoassay reagent)

IT 150-25-4, Bicine

RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (insol. carrier particle nephelometric immunoassay reagent)
 RN 150-25-4 HCAPLUS
 CN Glycine, N,N-bis(2-hydroxyethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1999:42620 HCAPLUS
 DOCUMENT NUMBER: 130:92468
 TITLE: Methods for covalent immobilization of biomolecules to a carrier by means of a His-tag
 INVENTOR(S): Bosman, Alfons; Van Wijnendaele, Frans; Van Den Broeck, Dirk; Van De Voorde, Andre
 PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

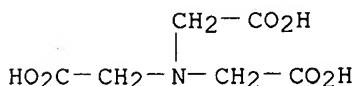
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900670	A1	19990107	WO 1998-EP3883	19980625
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9887290	A1	19990119	AU 1998-87290	19980625
AU 746325	B2	20020418		
EP 991944	A1	20000412	EP 1998-938647	19980625
PRIORITY APPLN. INFO.:			EP 1997-870095	A 19970625
			WO 1998-EP3883	W 19980625

AB The present invention relates to methods for covalent immobilization of biomols. to carriers and membranes, wherein the presence of a His-tag is exploited, and wherein the amino acid residues that comprise said His-tag are directly involved in the covalent bond. The present invention also provides several strategies that further augment the probability of covalent immobilization through said His-tags, such as improving the presentation of said His-tag, choosing the appropriate reaction conditions such as pH, temp., concn. of reagent and kinetics, increasing contact between His-tag and reactive groups of said carrier or membrane, by for instance the use of IDA or anti-His antibodies or increasing the

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document

hydrophobicity of the membrane, or shielding the rest of the biomol. from reaction by for instance increasing the hydrophobicity of said carrier or membrane or addn. of substrate or competitors or blocking otherwise reactive groups, or by choosing chem. reactions that have a high selectivity for histidine residues. A carrier can also be another biomol. The present invention thus also relates to a method that allows covalent crosslinking between identical or different biomols. When such biomols. have a natural tendency to interact with each other to form homo- or heterodimers, a strategy of increasing contact between the reactive groups (two His-tags or one His-tag and another reactive group) can be exploited. The present invention also relates to a method of providing a simultaneous and universal system for detection of biomols. through said His-tag.

IC ICM G01N033-547
 ICS C07K017-06; C12N011-06; C07K017-00; C12N011-00
 CC 9-9 (Biochemical Methods)
 Section cross-reference(s): 6
 IT **Immunoassay**
 (enzyme-linked immunosorbent assay; methods for covalent immobilization of biomols. to a carrier by means of a histidine His-tag)
 IT 100-42-5, Styrene, biological studies 139-13-9, NTA 142-73-4,
 IDA
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process);
 USES (Uses)
 (methods for covalent immobilization of biomols. to a carrier by means of a histidine His-tag)
 IT 108-31-6, Maleic anhydride, biological studies 111-30-8, Glutaraldehyde 616-02-4, Citraconic anhydride 816-39-7, 1,3-Dibromoacetone 25952-53-8, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride 109536-69-8, MMPP
 RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (methods for covalent immobilization of biomols. to a carrier by means of a histidine His-tag)
 IT 139-13-9, NTA
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process);
 USES (Uses)
 (methods for covalent immobilization of biomols. to a carrier by means of a histidine His-tag)
 RN 139-13-9 HCPLUS
 CN Glycine, N,N-bis(carboxymethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 5 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1997:794014 HCPLUS
 DOCUMENT NUMBER: 128:59173
 TITLE: Determination of rheumatoid factor by latex agglutination test

INVENTOR(S): Kusuba, Toshio
 PATENT ASSIGNEE(S): Sekisui Chemical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09318631	A2	19971212	JP 1996-137004	19960530
PRIORITY APPLN. INFO.:			JP 1996-137004	19960530
AB	Rheumatoid factor is detd. by treatment of a sample with human .gamma.-globulin-sensitized latex particles in the presence of .gtoreq.1 water-sol. compd. selected from trialkylamines, their salts, and quaternary ammonium salts and poly(vinylpyrrolidone) (I) and/or dextran, followed by measuring optical intensity. This method improves linearity of the relationship between the concns. of rheumatoid factor and the degree of agglutination. A 1st reagent (a phosphate buffer contg. BSA, NaCl, and I) and a 2nd reagent (a phosphate buffer contg. human .gamma.-globulin-sensitized polystyrene latex particles, choline chloride, BSA, and NaCl) were successively added to sample solns. of rheumatoid factor with various dilns., followed by measuring absorbance. Linearity of the calibration curve was good, while a control test using polyethylene glycol instead of I gave a sigmoid curve.			
IC	ICM G01N033-543 ICS G01N033-531; G01N033-564			
CC	9-10 (Biochemical Methods) Section cross-reference(s): 14			
IT	Rheumatoid factors RL: ANT (Analyte); ANST (Analytical study) (detn. of rheumatoid factor by latex agglutination test in presence of trialkylamines/quaternary ammonium salts and poly(vinylpyrrolidone)/dextran)			
IT	Quaternary ammonium compounds, analysis RL: ARU (Analytical role, unclassified); ANST (Analytical study) (detn. of rheumatoid factor by latex agglutination test in presence of trialkylamines/quaternary ammonium salts and poly(vinylpyrrolidone)/dextran)			
IT	Immunoassay (latex agglutination test ; detn. of rheumatoid factor by latex agglutination test in presence of trialkylamines/quaternary ammonium salts and poly(vinylpyrrolidone)/dextran)			
IT	Amines, analysis RL: ARU (Analytical role, unclassified); ANST (Analytical study) (tertiary ; detn. of rheumatoid factor by latex agglutination test in presence of trialkylamines/quaternary ammonium salts and poly(vinylpyrrolidone)/dextran)			
IT	Globulins, uses RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (.gamma.-, latex sensitized with human; detn. of rheumatoid factor by latex agglutination test in presence of triaalkylamines/quaternary ammonium salts and poly(vinylpyrrolidone)/dextran)			
IT	60-31-1, Acetylcholine chloride 67-48-1, Choline chloride 9003-39-8,			

Poly(vinylpyrrolidone) 9004-54-0, Dextran, analysis
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (detn. of rheumatoid factor by **latex agglutination**
 test in presence of trialkylamines/quaternary ammonium salts and
 poly(vinylpyrrolidone)/dextran)

L29 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:526270 HCAPLUS

DOCUMENT NUMBER: 127:202547

TITLE: Prevention of nonspecific reaction in immunoassay with
 masking agents, dispersants for filtration of feces,
 and immunoassay of filtrated samples

INVENTOR(S): Kikuchi, Tatsunori

PATENT ASSIGNEE(S): Eiken Chemical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09203735	A2	19970805	JP 1996-31406	19960125

PRIORITY APPLN. INFO.: JP 1996-31406 19960125

AB Nonspecific reaction in immunoassay caused by metal ions eluted from filter materials in filtration of samples is prevented by addn. of masking agents (e.g. complexons, phthalein complexons, oxines, and metal chelates) for metals in the samples. Suspended fecal samples are filtrated in the presence of chelating agents and/or metal chelates for immunoassay. Dispersants contg. chelating agents for filtration of suspended fecal samples are also claimed. The method prevents nonspecific reaction which is often obsd. in immunoassay for biol. samples after filtration with various filtration materials, e.g. paper filters, glass fiber filters, plastic filters, etc. Addn. of EDTA-2Na to HEPES buffer as a dispersant for feces samples suppressed nonspecific reaction in **latex agglutination** test for occult blood detection even after filtration of the dispersed samples with a glass fiber filter.

IC ICM G01N033-72

ICS G01N033-50; G01N033-543

CC 9-10 (Biochemical Methods)

IT Immunoassay

(agglutination test; prevention of nonspecific reaction in immunoassay caused by metal ions eluted from filters for filtration of biol. samples by masking agents)

IT 139-13-9, Nitrilotriacetic acid 139-33-3 150-25-4,

N,N-Bis(2-hydroxyethyl)glycine 150-39-0, N-(2-

Hydroxyethyl)ethylenediamine-N,N',N'-triacetic acid 817-11-8,

Nitrilotripropionic acid 4408-81-5, 1,2-Diaminopropane-N,N,N',N'-tetraacetic acid 6419-19-8, Nitrilotris(methylenephosphonic acid)

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (prevention of nonspecific reaction in immunoassay caused by contact of biol. samples with filters by masking agents)

IT 60-00-4, Ethylenediamine-N,N,N',N'-tetraacetic acid, uses 67-43-6

93-62-9 142-73-4, Iminodiacetic acid 482-54-2,

1,2-Cyclohexanediamine-N,N,N',N'-tetraacetic acid 1429-50-1,

Ethylenediamine-N,N,N',N'-tetrakis(methylenephosphonic acid) 1633-00-7

3148-72-9, 1,3-Diaminopropan-2-ol-N,N,N',N'-tetraacetic acid 5657-17-0,
 Ethylenediamine-N,N'-diacetic acid 13288-40-9, Ethylenediamine-N,N'-
 dipropionic acid 32701-19-2, Ethylenediaminediacetic acid dipropionic
 acid

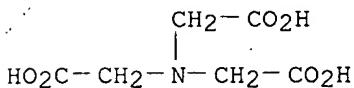
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (prevention of nonspecific reaction in immunoassay caused by metal ions
 eluted from filters for filtration of biol. samples by masking agents)

IT 139-13-9, Nitrilotriacetic acid 150-25-4,
 N,N-Bis(2-hydroxyethyl)glycine 817-11-8, Nitrilotripropionic
 acid

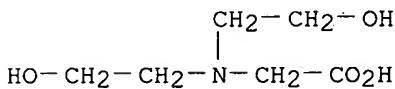
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (prevention of nonspecific reaction in immunoassay caused by contact of
 biol. samples with filters by masking agents)

RN 139-13-9 HCAPLUS

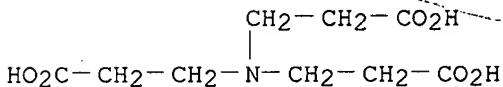
CN Glycine, N,N-bis(carboxymethyl)- (9CI) (CA INDEX NAME)



RN 150-25-4 HCAPLUS
 CN Glycine, N,N-bis(2-hydroxyethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 817-11-8 HCAPLUS
 CN .beta.-Alanine, N,N-bis(2-carboxyethyl)- (9CI) (CA INDEX NAME)

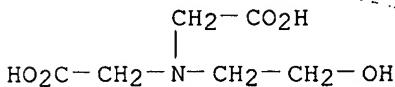


IT 93-62-9

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (prevention of nonspecific reaction in immunoassay caused by metal ions
 eluted from filters for filtration of biol. samples by masking agents)

RN 93-62-9 HCAPLUS

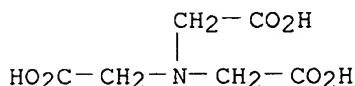
CN Glycine, N-(carboxymethyl)-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



L29 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1993:444697 HCAPLUS
 DOCUMENT NUMBER: 119:444697

TITLE: Buffer and latex agglutination
 method for hemoglobin detection in feces
 INVENTOR(S): Tsuji, Takashi
 PATENT ASSIGNEE(S): Nitto Denko Corp, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05099923	A2	19930423	JP 1991-292163	19911011
PRIORITY APPLN. INFO.:			JP 1991-292163	19911011
AB Hb in feces is detected by latex agglutination immunoassay using anti-human Hb antibody-sensitized latex and a buffer contg. chelator (e.g. EDTA) to suspend the feces sample. The chelator in the buffer inhibited Hb denaturation and thus stabilized the test sample for a prolonged time.				
IC	ICM	G01N033-531		
	ICS	G01N033-50; G01N033-53		
CC	9-10 (Biochemical Methods)			
IT	60-00-4, EDTA, uses 139-13-9, Nitrilotriacetic acid 139-33-3			
	RL:	USES (Uses)	(buffer contg., for Hb detection in feces by agglutination immunoassay)	
IT	139-13-9, Nitrilotriacetic acid			
	RL:	USES (Uses)	(buffer contg., for Hb detection in feces by agglutination immunoassay)	
RN	139-13-9 HCPLUS			
CN	Glycine, N,N-bis(carboxymethyl)- (9CI) (CA INDEX NAME)			



L29 ANSWER 8 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1989:530314 HCPLUS
 DOCUMENT NUMBER: 111:130314
 TITLE: Determination of human C-reactive protein by a
 latex agglutination test
 INVENTOR(S): Tanno, Kazunobu; Iijima, Hiromi; Kawagoe, Kiyotaka
 PATENT ASSIGNEE(S): Hitachi Chemical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63298061	A2	19881205	JP 1987-133076	19870528
JP 07107534	B4	19951115		

PRIORITY APPN. INFO.: JP 1987-133076 19870528

AB A sample is mixed with insol. carriers sensitized with anti-human C-reactive protein antibody and treated with a trialkylamine or its (quaternary ammonium) salts for agglutination; the optical d. is measured for human C-reactive protein detn. A sample was dild. with a soln. contg. choline chloride, NaCl and bovine serum albumin (in phosphate buffer, pH 6.5) and treated with antibody-sensitized polystyrene latex particles, and the reaction mixt. was measured at 570 nm for human C-reactive protein detn.

IC ICM G01N033-53
ICS G01N033-543

CC 9-10 (Biochemical Methods)

IT Proteins, specific or class
RL: ANT (Analyte); ANST (Analytical study)
(C-reactive, detn. of, by latex agglutination test,
triaalkylamines in, optical d. measurement in relation to)

IT Amines, uses and miscellaneous
RL: ANST (Analytical study)
(tertiary, in C-reactive protein detn. by agglutination test,
optical d. measurement in relation to)

L29 ANSWER 9 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:201348 HCPLUS
DOCUMENT NUMBER: 108:201348
TITLE: Reagents for quantitative determination of C-reactive protein
INVENTOR(S): Tanno, Kazunobu; Iijima, Hiromi; Kawagoe, Kyotaka
PATENT ASSIGNEE(S): Hitachi Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62218866	A2	19870926	JP 1986-62819	19860320
JP 05040868	B4	19930621		

PRIORITY APPN. INFO.: JP 1986-62819 19860320

AB Reagents for quant. detn. of C-reactive protein by latex agglutination tests consist of anti-human C-reactive protein antibody-sensitized insol. carriers and water-sol. compds. selected from trialkylamines, their salts, and quaternary ammonium salts. A sample was dild. with pH 6.5 phosphate buffer contg. choline chloride, NaCl and bovine serum albumin, and incubated with a reagent contg. 0.4% sensitized polystyrene latex particles at 37.degree., and the absorbance at 570 nm was monitored for C-reactive protein quantitation.

IC ICM G01N033-543
ICS G01N033-53.
CC 9-10 (Biochemical Methods)
IT Amines, compounds
RL: ANST (Analytical study)
(tertiary, C-reactive protein detn. by agglutination test
with reagents contg., enhanced sensitivity in relation to)

L29 ANSWER 10 OF 12 HCPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:201347 HCAPLUS
 DOCUMENT NUMBER: 108:201347
 TITLE: Rheumatoid factor determination by **latex**
agglutination tests
 INVENTOR(S): Tanno, Kazunobu; Iijima, Hiromi
 PATENT ASSIGNEE(S): Hitachi Chemical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62218865	A2	19870926	JP 1986-62818	19860320
JP 06068492	B4	19940831		

PRIORITY APPLN. INFO.: JP 1986-62818 19860320
 AB A sample contg. rheumatoid factor is mixed with human .gamma.-globulin-sensitized insol. carriers and .gtoreq.1 water-sol. compds. selected from polyethylene glycol, trialkylamine and their salts for agglutination, and the optical d. is measured for the quantitation of rheumatoid factor. A serum sample was dild. with 0.05M phosphate buffer contg. 0.9% polyethylene glycol and incubated with a reagent contg. human .gamma.-globulin-sensitized polystyrene latex at 37.degree. and measured at 570 nm for rheumatoid factor detn.

IC ICM G01N033-543
 ICS G01N033-564

CC 9-10 (Biochemical Methods)

IT **Amines, compounds**

RL: ANST (Analytical study)
 (tertiary, rheumatoid factor detn. by agglutination test with reagents contg., enhanced sensitivity in relation to)

L29 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:201346 HCAPLUS
 DOCUMENT NUMBER: 108:201346
 TITLE: Quantitative determination of human C-reactive protein by **latex** **agglutination** tests
 INVENTOR(S): Tanno, Kazunobu; Iijima, Hiromi; Kawagoe, Kyotaka
 PATENT ASSIGNEE(S): Hitachi Chemical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62218864	A2	19870926	JP 1986-62817	19860320
JP 05040867	B4	19930621		

PRIORITY APPLN. INFO.: JP 1986-62817 19860320
 AB A sample contg. human C-reactive protein is mixed with anti-C-reactive protein antibody-sensitized insol. carriers and water-sol. compds. selected from trialkylamine or salts for agglutination, and the optical d. is measured for quantitation. A sample was dild. with 0.05M phosphate

buffer contg. choline chloride, NaCl and bovine serum albumin, and incubated with a reagent contg. sensitized polystyrene latex particles at 37.degree., and the absorbance at 570 nm was measured for C-reactive protein detn.

IC ICM G01N033-543
ICS G01N033-53; G01N033-557

CC 9-10 (Biochemical Methods)

IT **Amines, compounds**

RL: ANST (Analytical study)
(**tertiary, C-reactive protein detn. by agglutination test with reagents contg., enhanced sensitivity in relation to**)

L29 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1987:172483 HCAPLUS

DOCUMENT NUMBER: 106:172483

TITLE: Aminocarboxylates and aminosulfonates as stabilizers for agglutination test reagents

INVENTOR(S): Kihara, Yasuo; Kawasaki, Takashi; Mori, Kenjiro; Ushiyama, Keiichi

PATENT ASSIGNEE(S): Nitto Electric Industrial Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61274261	A2	19861204	JP 1985-118586	19850530
PRIORITY APPN. INFO.:			JP 1985-118586	19850530
AB	The aminocarboxylates <u>A3-mN(BCO2H)</u> [A = H, (un)substituted alkyl; B = (un)substituted alkylene; m = 1 or 2; when m = 2, A .noteq. H] or the aminosulfonates <u>XYN2SO3H</u> [X, Y = H, (un)satd. alkyl, cycloalkyl, cycloamino; Z = (un)satd. alkylene; X = Y .noteq. H] are added to an aq. dispersion contg. sensitized, dispersible polymer particles (latex) to increase the reagent stability and agglutination test specificity.			

IC ICM G01N033-545

ICA A61K039-00

CC 9-10 (Biochemical Methods)

IT **Immunochemical analysis**

(**agglutination test, aminocarboxylates or aminosulfonates with latex reagents contg. sensitized and water-dispersible polymer particles for, to increase stability and specificity**)

IT Sulfonic acids, biological studies

RL: ANST (Analytical study)
(**amino, agglutination test latex reagents contg., to increase stability and specificity**)

IT Carboxylic acids, biological studies

RL: ANST (Analytical study)
(**iminodi-, agglutination test latex reagents contg., to increase stability and specificity**)

IT Amino acids, biological studies

RL: ANST (Analytical study)
(**.omega.-, agglutination test latex reagents contg., to increase stability and specificity**)

IT 103-47-9, 150-25-4 1132-61-2 1135-40-6 4432-31-9
5625-37-6 5704-04-1 7365-82-4 10191-18-1 26239-55-4 68189-43-5
68399-77-9 68399-80-4 107900-92-5 107900-93-6 107900-94-7

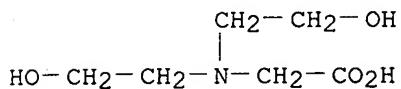
RL: ANST (Analytical study)
(agglutination test latex reagents contg., to
increase stability and specificity)

IT 150-25-4

RL: ANST (Analytical study)
(agglutination test latex reagents contg., to
increase stability and specificity)

RN 150-25-4 HCPLUS

CN Glycine, N,N-bis(2-hydroxyethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)



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L4

STR

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G1

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Ak[^] G2
@5 6Ak[^] O[~] Ak[^] G2
@7 8 9 10O[~] Ak
@11 12S[~] Ak
@13 14G1[~] N[~] G1
1 2 3O⁼⁼ C[~] O
15 @16 17O⁼⁼ C[~] O[~] Ak
18 @19 20 21O⁼⁼ C[~] N[~] Ak
22 @23 24 25

VAR G1=5/7

VAR G2=OH/11/13/16/19/23

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 2
 CONNECT IS E2 RC AT 5
 CONNECT IS E2 RC AT 7
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 CONNECT IS E1 RC AT 12
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 CONNECT IS E1 RC AT 21
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 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L6 405652 SEA FILE=REGISTRY ABB=ON PLU=ON (((N AND C AND O AND H)/ELS
 AND 4/ELC.SUB) OR ((N AND C AND S AND H)/ELS AND 4/ELC.SUB) OR
 ((N AND C AND O AND S AND H)/ELS AND 5/ELC.SUB)) AND NC=1 NOT
 RSD/FA
 L11 651 SEA FILE=REGISTRY SUB=L6 SSS FUL L4
 L37 2145 SEA L11
 L38 19124 SEA TERT?(2A) AMINE
 L39 101 SEA (L37 OR L38) AND (CDI OR CARBODIIMID? OR (PARTICL? OR
 LATEX) (5A) (AGGLUT? OR FIX?))
 L40 9 SEA L39 AND (IMMUNO? OR ASSAY?)
 L41 9 DUP REM L40 (0 DUPLICATES REMOVED)

=> @ 141 bibb.abs 1-9

L41 ANSWER 1 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
 ACCESSION NUMBER: 2003-646011 [61] WPIX
 DOC. NO. CPI: C2003-176727
 TITLE: New tyrosyl piperazine derivatives are purinergic P2X7
 receptor modulators, useful for treating e.g. rheumatoid
 arthritis, cancer, lupus erythematosus.

DERWENT CLASS: B02 B03
 INVENTOR(S): BARALDI, P G; BOREA, P A
 PATENT ASSIGNEE(S): (BARA-I) BARALDI P G; (BORE-I) BOREA P A; (KING-N) KING
 PHARM RES & DEV INC
 COUNTRY COUNT: 100
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003059353	A1	20030724	(200361)*	EN	34
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2003181452 A1 20030925 (200364)					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003059353	A1	WO 2002-US41385	20021223
US 2003181452	Provisional	US 2001-342977P	20011221
		US 2002-329094	20021223

PRIORITY APPLN. INFO: US 2001-342977P 20011221; US 2002-329094
 20021223
 AN 2003-646011 [61] WPIX
 AB WO2003059353 A UPAB: 20030923
 NOVELTY - Tyrosyl piperazine derivatives (I)-(IV) are new.
 DETAILED DESCRIPTION - Tyrosyl piperazine derivatives of formula (I)-(IV) and their salts are new.
 R₁, R₂ = 1-4C alkyl or 1-4C alkoxy (both optionally substituted), H, 1-4C acyl, halo, NO₂, NH₂ or (di)alkylamino;
 R₃-R₈ = CH or N;
 R₉ = H or Me;
 R₁₀ = CO or (CH₂)_n;
 n, n' = 0-4;
 R₁₁, R₁₂ = N or CH;
 X₁, X₂ = H, deuterium, tritium or halo;
 X₃ = N or CH;
 R_{1a}, R_{2a} = H, 1-4C alkyl, 1-4C alkoxy, 1-4C acyl, halo, CN, NO₂, NH₂, or (di)alkylamino; and
 R_{1b}, R_{2b} = H, 1-4C alkyl, 1-4C alkoxy, halo, CN, NO₂ or NH₂;
 provided that when n' = 0, R_{1b} and R_{2b} are not both H.
 ACTIVITY - Antinflammatory; Immunosuppressive;
 Antirheumatic; Antiarthritic; Tuberculostatic; Antiinfertility;
 Dermatological; Cytostatic; Vulnerary.
 MECHANISM OF ACTION - Purinergic P2X7 Receptor Modulator.
 Adenosine triphosphate (ATP) dependent increases in plasma membrane permeability were measured with extracellular fluorescent tracer ethidium bromide. For ethidium bromide uptake cells were incubated in a thermostat-controlled fluorometer cuvette (37 deg. C) for 20 minutes in the dark at concentration of 1000000 cells/ml in the presence of ethidium bromide (20 mM) and challenged with ATP (1 mM). Cell suspension was

incubated with 1-((S)-N,O-bis(isoquinolinesulfonyl)-N-methyl-tyrosyl)-4-(4-fluorophenyl)piperazine (IVa) (25-5000 nM) for 5 minutes at 37 deg. C before fluorimetric analysis in a stirred cuvette at 37 deg. C.

Fluorescence changes were monitored at the wavelength pair 360/580 nm. After several washing to remove extracellular dye, cells were analyzed with an inverted fluorescence microscope. (IVa) Inhibited ATP dependent increases in plasma membrane permeability with an IC₅₀ of 1.33 nM.

USE - For inducing apoptosis in neoplastic cell and in treating medical conditions (e.g. inflammatory disease, disease of immune system, rheumatoid arthritis, tuberculosis, sterility, inflammatory bowel disease, lupus erythematosus, organ transplant, cancer and wound) in a human (claimed).

Dwg.0/4

L41 ANSWER 2 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-692243 [66] WPIX

DOC. NO. CPI: C2003-190361

TITLE: New benzamide derivative or its salts, useful for preventing and treating diseases such as osteoporosis, diabetes, hyperlipidemia and arteriosclerosis, has peroxisome proliferator activated receptor modulator activity.

DERWENT CLASS: B05

PATENT ASSIGNEE(S): (SANY) SANKYO CO LTD

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2003128639 A		20030508	(200366)*		49

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2003128639 A		JP 2001-327197	20011025

PRIORITY APPLN. INFO: JP 2001-327197 20011025

AN 2003-692243 [66] WPIX

AB JP2003128639 A UPAB: 20031014

NOVELTY - Novel benzamide derivatives (I) and their salts.

DETAILED DESCRIPTION - New benzamide derivatives of formula (I), and their salts.

A = H, amino group, 1-12C alkylamino, 2-8C alkanoyl amino, 1-6C alkoxy, hydroxy, mercapto, carboxy, 2-7C alkyloxycarbonyl, sulfonyl, 1-6C alkylsulfonyl, 1-6C alkyl or heterocyclyl (substituted with one or more amino or hydroxy);

Alk = 1-6C alkylene group;

B = single bond, aryl, cycloalkyl or heterocyclyl (all optionally substituted with (alpha) 1-6C alkyl, nitro, cyano, carboxy, 2-7C alkyloxycarbonyl, 3-15C alkyloxycarbonylalkyl or amino (optionally substituted with 3-6C alkenyl, halo, 1-6C haloalkyloxy, 1-6C alkoxy, 1-6C alkylthio, amidino-aminosulfonyl or phenyl;

R1 = H, 1-6C alkyl or aralkyl; and

X1,X2 = single bond, O, S, CO, N, SO₂N, NSO₂, CONH or NHCO.

ACTIVITY - Osteopathic; Antidiabetic; Anorectic;

Antiarteriosclerotic; Antilipemic; Antiinflammatory; Immunosuppressive; Cytostatic; Hepatotropic; Vasotropic; Cardiant; Nootropic; Neuroprotective; Hypotensive; Nephrotropic. 8-week-old Syrian golden hamster male rats were ingested with a diet containing 0.3% (weight/weight) of N-(2-(4-(phenyl sulfonyl amino) phenyl) ethyl)-(2-chloro-5-nitrophenyl) carboxamide for 1 week. After 1 week, the total high density lipoprotein cholesterol (HDL-TC) and free HDL cholesterol (HDL-FC), were evaluated in HDL fraction using HDL cholesterol precipitate test reagent. The HDL-TC and HDL-FC were found to be 107.4% and 135.2%, respectively. The results concluded the compound exhibited remarkable antiarteriosclerotic effect.

MECHANISM OF ACTION - PPAR-Agonist-Gamma; Leptin-Agonist. Fat tissues extracted from wister imamichi male rat (6-week-old) was mixed with of Hanks liquid 1 ml containing of collagenase (10 mg), shaken for 50 minutes and incubated at 90 rpm and 37 deg. C. 20 ml of Hanks liquid was then mixed, filtered and centrifuged for 1 minute at 1000 rpm. Fat cell suspension (60 ml) was then mixed with of culture medium (100 micro l) and of N-(1-phenyl ethyl)-(2-chloro-5-nitrophenyl) carboxamide (1 micro l) and incubated for 1 hour or more at 30 deg. C. The leptin concentration was measured by enzyme linked immunosorbant assay (ELISA) method using rat leptin measurement kit-IBL. The leptin production was 109.4%, thus demonstrating that the test compound exhibited excellent leptin-agonist effect.

USE - For preventing and treating osteoporosis, diabetes, obesity, arteriosclerosis, hyperlipidemia, abnormality in lipid metabolism, pancreatitis, autoimmune diseases, hyperuricemia, leukemia, abnormality in liver function, ischemia, cancer, inflammation, Basedow's disease, cardiac disease, Alzheimers disease, eating disorders, hypertension and renal diseases.

ADVANTAGE - The new benzamide derivatives having excellent peroxisome proliferator activated receptor-(gamma) modulator activity is effectively used in preventing and treating osteoporosis. The benzamide derivative or its salts can be manufacture easily and effectively with improved yield.

Dwg.0/3

L41 ANSWER 3 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-723291 [69] WPIX

DOC. NO. NON-CPI: N2003-578338

DOC. NO. CPI: C2003-199176

TITLE: **Immunoassay** reagent comprising particles with a surface activated by a carbodiimide and linked to a binding agent, and a tertiary amine compound useful for preventing non-specific interactions in particle agglutination immunoassays.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): LAWRENCE, C C; SHANAFELT, A B

PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE DIAGNOSTICS GMBH; (LAWR-I) LAWRENCE C C; (SHAN-I) SHANAFELT A B

COUNTRY COUNT: 33

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1321770	A2	20030625	(200369)*	EN	13

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC
 MK NL PT RO SE SI SK TR
 CA 2414704 A1 20030618 (200369) EN
 JP 2003207512 A 20030725 (200369) 36
 US 2003138974 A1 20030724 (200369)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1321770	A2	EP 2002-27992	20021214
CA 2414704	A1	CA 2002-2414704	20021217
JP 2003207512	A	JP 2002-363686	20021216
US 2003138974	A1	US 2001-25378	20011218

PRIORITY APPLN. INFO: US 2001-25378 20011218

AN 2003-723291 [69] WPIX

AB EP 1321770 A UPAB: 20031027

NOVELTY - A reagent for use in **immunoassays** comprising multiple particles, each having a surface activated by a **carbodiimide**, a binding agent linked to the surface through a covalent bond, and a **tertiary amine** compound, is new.

DETAILED DESCRIPTION - A reagent (R) for use in **immunoassays**, comprises multiple particles, each having a surface activated by a **carbodiimide**, a binding agent linked to the surface through a covalent bond, and a **tertiary amine** compound of formula (I).

N(R1-X)(R2-Y)(R3-Z) (I),
 where R1, R2 and R3 are independently chosen from alkyl and alkyl ether; and

X, Y, and Z are independently chosen from -OH, -O-R4, -S-R4, -C(=O)-OH, -C(=O)-OR4, and -C(=O)-NHR4, where R4 is alkyl.

INDEPENDENT CLAIMS are also included for:

(1) a test kit comprising (R);
 (2) an **immunoassay** method (M1), in which a sample suspected of containing an analyte is combined with (R), where the improvement comprises the addition of the **tertiary amine** of formula (I); and

(3) use of a **tertiary amine** compound of formula (I) in **particle-based agglutination immunoassay** to prevent non-specific interactions.

USE - (R) is useful in **particle-based agglutination immunoassays**, the **tertiary amine** helping to prevent non-specific interactions (claimed).

ADVANTAGE - (R) improves the accuracy of **particle-based agglutination immunoassays** by reducing or eliminating non-specific interactions.

DESCRIPTION OF DRAWING(S) - The figure shows the graph of the dependence of the absorbance at 468 nm due to bound orange 7 dye as a function of particle concentration.

Dwg.1/4

L41 ANSWER 4 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
 ACCESSION NUMBER: 2002-519057 [55] WPIX
 DOC. NO. NON-CPI: N2002-410923
 DOC. NO. CPI: C2002-146734

TITLE: New biodegradable, blood-compatible biopolymer comprising crosslinked polyubiquitin, forming hydrogels or matrices useful e.g. as wound dressings, drug delivery vehicles or enzyme biosensors.

DERWENT CLASS: A96 B04 P34

INVENTOR(S): BOSSE, M

PATENT ASSIGNEE(S): (VIRI-N) VIRIDIS BIOTECH INC; (BOSS-I) BOSSE M

COUNTRY COUNT: 97

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001091814	A2	20011206	(200255)*	EN	75
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001067181	A	20011211	(200255)		
EP 1284992	A2	20030226	(200319)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2003114724	A1	20030619	(200341)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001091814	A2	WO 2001-CA784	20010529
AU 2001067181	A	AU 2001-67181	20010529
EP 1284992	A2	EP 2001-944783	20010529
		WO 2001-CA784	20010529
US 2003114724	A1	WO 2001-CA784	20010529
		US 2002-275985	20021120

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001067181	A Based on	WO 2001091814
EP 1284992	A2 Based on	WO 2001091814

PRIORITY APPLN. INFO: US 2000-207325P 20000530; US 2002-275985
20021120

AN 2002-519057 [55] WPIX

AB WO 2001091814 A UPAB: 20030919

NOVELTY - A novel biopolymer (A) comprises a 3-dimensionally crosslinked mixture of ubiquitin (I) (a small protein having a sequence of 76 amino acids given in the specification) and at least one crosslinking agent (II).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) preparation of (A);
(ii) a biopolymer comprising (I), a solvent for (I) and at least one (II); and
(iii) the use of (I) in the preparation of (A).

ACTIVITY - Hemostatic; vulnerary.

MECHANISM OF ACTION - None given in the source material.

USE - (A) form hydrogels or matrices useful as wound dressings, biodegradable vehicles for oral, parenteral or topical drug delivery, enzyme biosensors for detection of nucleic or peptide molecules, in situ hybridization systems (e.g. for use in diagnostic assays), in vitro model systems for research, hemostatic agents, prostheses or implants (possibly containing cell cultures).

ADVANTAGE - (A) are biodegraded to non-toxic, endogenous materials; have good blood compatibility and low immunogenicity and can be prepared with a wide range of controllable properties (e.g. hydrophilicity, charge, degree of crosslinking, drug uptake and degradation/release kinetics).

Dwg. 0/18

L41 ANSWER 5 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-055454 [07] WPIX

DOC. NO. CPI: C2002-015870

TITLE: Purification compound for making pure immunoglobulins for therapeutic and diagnostic applications, includes non-peptidic ligand attached to support matrix.

DERWENT CLASS: A11 A25 A96 B04

INVENTOR(S): GRIFFIN, M; SCARPA, I; STIPANOVIC, B

PATENT ASSIGNEE(S): (ACCU-N) ACCURATE POLYMERS INC; (ACCU-N) ACCURATE POLYMERS LTD; (GRIF-I) GRIFFIN M; (SCAR-I) SCARPA I; (STIP-I) STIPANOVIC B

COUNTRY COUNT: 96

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
<hr/>					
WO 2001083515	A2	20011108	(200207)*	EN	23
RW:	AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ				
NL OA PT SD SE SL SZ TR TZ UG ZW					
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK				
DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ					
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD					
SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
US 2001045384	A1	20011129	(200207)		
AU 2001059293	A	20011112	(200222)		
EP 1276557	A2	20030122	(200308)	EN	
R:	AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT				
RO SE SI TR					
US 6572767	B2	20030603	(200339)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
<hr/>			
WO 2001083515	A2	WO 2001-US13970	20010430
US 2001045384	A1 Provisional	US 2000-200591P	20000428
		US 2001-846471	20010430
AU 2001059293	A	AU 2001-59293	20010430
EP 1276557	A2	EP 2001-932794	20010430
		WO 2001-US13970	20010430
US 6572767	B2 Provisional	US 2000-200591P	20000428
		US 2001-846471	20010430

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001059293 A	Based on	WO 2001083515
EP 1276557	A2 Based on	WO 2001083515

PRIORITY APPLN. INFO: US 2000-200591P 20000428; US 2001-846471
20010430

AN 2002-055454 [07] WPIX

AB WO 200183515 A UPAB: 20020130

NOVELTY - A purification compound comprises a support matrix and a non-peptidic ligand.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for (A) a method of manufacturing the ligand compounds of formulae (I), (II), (III), and (IV); and (B) a purification method comprising providing the specified support matrix having a non-peptidic ligand, introducing the support matrix to a solution containing a target compound, allowing for an interaction to occur between the ligand and the target compound, washing the beads having a ligand to the target compound so that the target compound is eluted from the solution. The support matrix is reusable. Formula (I) is manufactured by reacting 2-anilino-4,6-dichloro-s-triazine with a molecular super-structure having a terminal hydrazide functional group. Formula (II) is manufactured by reacting a (4' hydroxy)phenetylaldo-1-carboxy-anilido-3-carboxyphenyl-5-amine with a terminal, activated ester functional group, or reacting a 5-amino bisamide with a carbonyl group. Formula (III) is manufactured by reacting a 5-amino bisamide with a carbonyl group, or reacting a (a(4, hydroxy)phenetylaldo-1-carboxy-anilido-3-carboxyphenyl-5-amine with a terminal **tertiary** dicarboxy-ethyl **amine** in the presence of a peptide-coupling agent. Formula (IV) is manufactured by reacting a primary amino group on a spacer arm with a triepoxy compound to form a terminal diepoxy compound, and reacting the terminal diepoxy compound with a mercaptoheterocyclic compound.

USE - For making pure **immunoglobulins** for therapeutic and diagnostic applications.

ADVANTAGE - The large-scale purification of bio-molecules and, in particular, **immunoglobulines**, is accomplished by using a cellulose bead attached to small, non-peptidic compounds which display a high affinity and selectivity for the biomolecule to be purified. The beads with the attached ligands of formulae (I-IV) also possess a high chemical stability under rigors of recycling and sterilization.

Dwg. 0/0

L41 ANSWER 6 OF 9 WPIX COPYRIGHT 2003 THOMSON.DERWENT on STN
ACCESSION NUMBER: 1999-215021 [18] WPIX
DOC. NO. CPI: C1999-063354
TITLE: Preparation of 5,6-dihydro-4-hydroxy-2H-pyran-2-one derivatives useful as intermediates for antiviral agent.
DERWENT CLASS: B03
INVENTOR(S): GAGE, J R; HEWITT, B D; KELLY, R C
PATENT ASSIGNEE(S): (PHAA) PHARMACIA & UPJOHN CO
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 9912919 A1 19990318 (199918)* EN 45
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
 GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
 US UZ VN YU ZW
 AU 9892965 A 19990329 (199932)
 FI 2000000553 A 20000310 (200028)
 NO 2000001274 A 20000510 (200034)
 EP 1015441 A1 20000705 (200035) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 US 6077963 A 20000620 (200035)
 CZ 2000000804 A3 20000816 (200048)
 SK 2000000226 A3 20001009 (200056)
 CN 1268947 A 20001004 (200067)
 HU 2000003593 A2 20010228 (200121)
 US 6265604 B1 20010724 (200146)
 MX 2000002411 A1 20001001 (200158)
 KR 2001023864 A 20010326 (200161)
 JP 2001515895 W 20010925 (200170) 53
 AU 743496 B 20020124 (200221)
 NZ 503338 A 20020301 (200224)
 NZ 516325 A 20021220 (200309)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9912919	A1	WO 1998-US17993	19980903
AU 9892965	A	AU 1998-92965	19980903
FI 2000000553	A	WO 1998-US17993	19980903
		FI 2000-553	20000310
NO 2000001274	A	WO 1998-US17993	19980903
		NO 2000-1274	20000310
EP 1015441	A1	EP 1998-945806	19980903
		WO 1998-US17993	19980903
US 6077963	A Provisional	US 1997-58618P	19970911
	Cont of	US 1998-146406	19980903
		US 1998-213887	19981217
CZ 2000000804	A3	WO 1998-US17993	19980903
		CZ 2000-804	19980903
SK 2000000226	A3	WO 1998-US17993	19980903
		SK 2000-226	19980903
CN 1268947	A	CN 1998-808711	19980903
HU 2000003593	A2	WO 1998-US17993	19980903
		HU 2000-3593	19980903
US 6265604	B1 Provisional	US 1997-58618P	19970911
	Cont of	US 1998-146406	19980903
	Div ex	US 1998-213887	19981217
		US 2000-514087	20000228
MX 2000002411	A1	MX 2000-2411	20000309
KR 2001023864	A	KR 2000-702546	20000310
JP 2001515895	W	WO 1998-US17993	19980903
		JP 2000-510727	19980903

AU 743496	B	AU 1998-92965	19980903
NZ 503338	A	NZ 1998-503338	19980903
		WO 1998-US17993	19980903
NZ 516325	A Div ex	NZ 1998-503338	19980903
		NZ 1998-516325	19980903

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9892965	A Based on	WO 9912919
EP 1015441	A1 Based on	WO 9912919
CZ 2000000804	A3 Based on	WO 9912919
HU 2000003593	A2 Based on	WO 9912919
JP 2001515895	W Based on	WO 9912919
AU 743496	B Previous Publ.	AU 9892965
	Based on	WO 9912919
NZ 503338	A Div in	NZ 516325
	Based on	WO 9912919
NZ 516325	A Div ex	NZ 503338

PRIORITY APPLN. INFO: US 1997-58618P 19970911; US 1998-146406
 19980903; US 1998-213887 19981217; US
 2000-514087 20000228

AN 1999-215021 [18] WPIX

AB WO 9912919 A UPAB: 20011203

NOVELTY - 5,6-Dihydro-4-hydroxy-2H-pyran-2-one derivatives (CVI) are prepared by reacting the activated form of a 3-hydroxypropanoic acid derivative (CIV') with a malonate monoester and a divalent metal then contacting with an acid followed by a base (B2) in the presence of a 1-4C alcohol, tetrahydrofuran or dimethylformamide.

DETAILED DESCRIPTION - Preparation of 5,6-dihydro-4-hydroxy-2H-pyran-2-one derivatives of formula (CVI) comprises:

(a) contacting a 3-hydroxypropanoate salt of formula (CIV) with an acid (A1);
 (b) extracting the free acid (CIV') formed;
 (c) contacting (CIV') with an activating agent and optionally a base (B1);
 (d) reacting with malonate monoester (MME) and a divalent metal;
 (e) contacting with an acid (A2); and
 (f) contacting with a base (B2) in the presence of a 1-4C alcohol, tetrahydrofuran or dimethylformamide.

R1, R2 = 1-6C alkyl, cyclohexyl, phenyl or $\text{CH}_2\text{CH}_2\text{Ar}$;
 Ar = phenyl substituted by R11;
 R11 = optionally protected hydroxy, optionally protected amino, H, NHCOMe or N(COMe)2.

INDEPENDENT CLAIMS are also included for the following:
 (A) preparation of (CVI) in which steps (a) - (c) are replaced by contacting (CIV), or its free acid form, with an activating agent;
 (B) (R)-3-hydroxy-3-(2-phenylethyl)hexanoic acid (CIV'a) and its salts (preferably the hydroxide, ammonia, tromethamine (THAM) 2-amino-2-hydroxymethyl-1,3-propanediol, (1R,2S)- or (1S,2R)-norephedrine, (R)- or (S)-2-amino-2-phenylethanol, or (R) or (S)-1-phenylethylamine salt);
 (C) (6R)-5,6-dihydro-4-hydroxy-6-(2-phenylethyl)-6-propyl-2H-pyran-2-one (CVIa);
 (D) (3 alpha (R),6(R))-5,6-dihydro-4-hydroxy-3-(1-(3-nitrophenyl)-

propyl)-6-(2-phenylethyl)-6-propyl-2H-pyran-2-one (XVII);
 (E) (S)-methyl 3-(3-nitrophenyl)pentanoate (XIII); and
 (F) (3 alpha (R),6(R))-5,6-dihydro-4-hydroxy-3-((Z)-1-(3-nitrophenyl)propenyl)-6-(2-phenylethyl)-6-propyl-2H-pyran-2-one (XXV).

USE - The compounds are intermediates for (R-(R(asterisk),R(asterisk))-N-(3-(1-(5,6-dihydro-4-hydroxy-2-oxo-(6-(2-phenylethyl)-6-propyl-2H-pyran-2-yl)propyl)phenyl)-5-trifluoromethyl-2-pyridinesulfonamide (XIX) useful as a retroviral protease inhibitor for treating human **immunodeficiency** virus (HIV) (see WO9230670 and WO9411361), human T-cell leukemia virus, and symptomatic acquired immune deficiency syndrome (AIDS).

(CVIa) is an intermediate for (XXV) which is an intermediate for (XVII) which is an intermediate for (XIX).

ADVANTAGE - The process produces (CVI) in optically pure form.

Dwg.0/0

L41 ANSWER 7 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
 ACCESSION NUMBER: 1995-284907 [38] WPIX
 DOC. NO. NON-CPI: N1995-216913
 DOC. NO. CPI: C1995-128577
 TITLE: Quaternary ammonium conjugates for use in immunoassays - also for eliciting antibodies and determination of hapten(s) contg. a tertiary amine, e.g. drugs of abuse.
 DERWENT CLASS: B04 B05 D16 S03
 INVENTOR(S): CRAIG, A R
 PATENT ASSIGNEE(S): (DADE-N) DADE CHEMISTRY SYSTEMS INC; (DUPO) DU PONT DE NEMOURS & CO E I; (DADE-N) DADE BEHRING INC
 COUNTRY COUNT: 5
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 668504	A1	19950823	(199538)*	EN	20
	R: DE FR IT				
JP 07260784	A	19951013	(199550)		14
US 5492841	A	19960220	(199613)		10
JP 2731739	B2	19980325	(199817)		13
EP 668504	B1	20010321	(200117)	EN	
	R: DE FR IT				
DE 69520383	E	20010426	(200130)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 668504	A1	EP 1995-101210	19950130
JP 07260784	A	JP 1995-29300	19950217
US 5492841	A	US 1994-199380	19940218
JP 2731739	B2	JP 1995-29300	19950217
EP 668504	B1	EP 1995-101210	19950130
DE 69520383	E	DE 1995-620383	19950130
		EP 1995-101210	19950130

FILING DETAILS:

PATENT NO	KIND	PATENT NO
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JP 2731739 B2 Previous Publ. JP 07260784
 DE 69520383 E Based on EP 668504

PRIORITY APPLN. INFO: US 1994-199380 19940218

AN 1995-284907 [38] WPIX

AB EP 668504 A UPAB: 19960829

Quaternary ammonium conjugate of formula (I), are useful in immunoassays and/or eliciting antibodies for determining the presence and/or amt. of a hapten in a test sample. The hapten has a **tert. amine gp.** or can be derivatised to a **tert. amine gp.** [(Q+-L-Z-)-M]B- (I). Q = a quat. ammonium gp. cyclic or acyclic, contg. a **tert. amine gp.** present in the hapten or its deriv.; L = a linker contg. 0-20C and hetero atoms arranged in a chain and/or ring structure provided that there are not more than than 6 heteroatoms and that not more than 2 are linked in sequence; Z = -C=O-, -CH=, -N=N-, -NH-, -NMe-, -NH-S=C-, -SO2-, -OC=O- or -C=O-NH-NH2-; x = 1; and B = an anion. In the subsequent prepn. claim, the link to the carrier (L-Z) has 0-40C and heteroatoms. Also claimed is an antibody raised against the conjugate (I).

USE - (I) is of use in **assay** of drugs contg. a **tert. amine gp.** or those which can be derivatised to a **tert. amine gp.** This gp. can be quaternised and linked to the carrier to provide (I). The drugs include drugs of abuse, e.g. amphetamines, barbiturates, benzodiazepams, cocaine, methadone, methaqualone, opiates, phencyclidine, propoxyphene, tetrahydrocannabinol and their related structures; also other drugs, e.g. quinidine, procanimide and N-acetylprocanimide or tricyclic amine antidepressants. Detection and determin. of these is either by conjugation with an **immunogen** for an **immunoassay** or with a reporter contg. gp., e.g. fluorescent or chemiluminescent. The **immunoassays** include ELISA, sandwich, fluorescence polarisation, nephelometric or particle based **agglutination** types. (I) can also be injected into animal hosts to stimulate antibody prodn. and the latter harvested for use in binding reactions, opt. after purifcn. by e.g. affinity chromatography with haptens for their detection and determination with high specificity.

ADVANTAGE - (I) are stated to offer significant advantages over known **immunogenic** conjugates and reporter reagents, without these being specified.

Dwg. 0/0

ABEQ US 5492841 A UPAB: 19960329

A quaternary ammonium conjugate useful for eliciting antibodies to a non-quaternary ammonium hapten or in an **immunoassay** for determining the presence and/or amount in a test sample of a non-quaternary ammonium hapten, the quaternary ammonium conjugate comprising compounds of the formula $((Q(+)-L-Z)xM)B^-$ wherein

Q⁺ is a quaternary ammonium group, cyclic or acyclic, derived by covalent attachment of a linker to a hapten selected from the group consisting of cocaine, methadone, methaqualone, propoxyphenes, phencyclidine, amphetamine, benzodiazepams, quinidine, procanimide, N-acetyl procanimide, and tricyclic amines; L is a linker comprising from 0 to 20 carbon atoms and heteroatoms arranged in a straight or branched chain and/or containing ring structures, with no more than a total of 6 heteroatoms and with no more than two heteroatoms linked in sequence; Q⁺ is linked to L at the **tertiary amine group** of the hapten; -Z- is a residue group selected from the group consisting of -C=O,

$-\text{CH}=$, $-\text{N}=\text{N}-$, $-\text{NH}-$, $-\text{NCH}_3$, $-\text{NH}-\text{S}=\text{C}$, $-\text{SO}_2-$, $-\text{O}-\text{C}=\text{O}$, and $-\text{C}=\text{O}-\text{NH}-\text{NH}_2-$; x is greater than or equal to 1; M is a carrier selected from the group consisting of poly(amino)acids, carbohydrates, yeasts, polysaccharides and solid phase particles; B- is an anion; and $(\text{Q}(+)-\text{L}-\text{Z})\text{x}^-$ is covalently bound to M.

Dwg. 0/0

L41 ANSWER 8 OF 9 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
 ACCESSION NUMBER: 1986-260397 [40] WPIX
 DOC. NO. NON-CPI: N1986-194558
 DOC. NO. CPI: C1986-112598
 TITLE: Prepn. of carriers for enzyme immunoassay - by treating polyacrylamide holding antigen or antibody with carbo di imide and guanidine salt or urea.
 DERWENT CLASS: A96 B04 D16 S03
 PATENT ASSIGNEE(S): (IGAK-N) IGAKU SEIBUTUGAKU K
 COUNTRY COUNT: 1
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 61186857	A	19860820	(198640)*		5
JP 05064739	B	19930916	(199341)		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 61186857	A	JP 1985-28546	19850214
JP 05064739	B	JP 1985-28546	19850214

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 05064739	B Based on	JP 61186857

PRIORITY APPLN. INFO: JP 1985-28546 19850214

AN 1986-260397 [40] WPIX

AB JP 61186857 A UPAB: 19930922

The process comprises treating carrier of polyacrylamide holding an antigen or antibody with one or two of the cpds. of formula $\text{R}_1-\text{N}=\text{C}=\text{N}-\text{R}_2\text{R}_3$ (I), and then treating the carrier with a guanidine salt or urea (where R_1 is a monovalent hydrocarbon gp.; R_2 is a divalent hydrocarbon gp.; R_3 binding to R_2 represents amino forming a tert-amine).

Enzyme immunoassay comprises binding an antibody or antigen to be assayed to the first antigen or antibody held on the carrier, then binding a prefixed amt. of enzyme-labelled 2nd antigen or antibody to the antibody or antigen bound to the carrier, and measuring the activity of the 2nd antigen or antibody bound or not bound to the carrier.

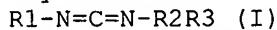
Polyacrylamide as carrier may be used in a large-surface form, e.g. granules, pieces, fibre, partic. gelled polyacrylamide used in gel column chromatography. Use of carbodiimides (I) is effective in fixing an antigen or antibody on the carrier. The antigen or antibody-fixed carrier is further treated with guanidine hydrochloride or urea for further stabilisation.

ADVANTAGE - Any antigen or antibody can be fixed stably on the carriers. Stable and qualified carriers used in enzyme **immunoassay** can be prep'd. on a large scale. By using the carriers, enzyme **immunoassay** (EIA) can be made accurately with reduced error.

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ABEQ JP 93064739 B UPAB: 19931130

Process comprises treating carrier of polyacrylamide holding an antigen or antibody with one or two of the cpds. of formula



and then treating the carrier with a guanidine salt or urea. In (I), R1 is a monovalent hydrocarbon gp.; R2 is a divalent hydrocarbon gp.; R3 binding to R2 represents amino forming a **tert.-amine**.

Enzyme **immunoassay** comprises binding an antibody or antigen to be **assayed** to the first antigen or antibody held on the carrier, then binding a prefixed amt. of enzyme-labelled 2nd antigen or antibody to the antibody or antigen bound to the carrier, and measuring the activity of the 2nd antigen or antibody bound or not bound to the carrier.

Polyacrylamide as carrier may be used in a large-surface form, e.g., granules, pieces, fibre, partic. gelled polyacrylamide used in gel column chromatography. Use of **carbodiimides** (I) is effective in fixing an antigen or antibody on the carrier. The antigen or antibody-fixed carrier is further treated with guanidine hydrochloride or urea for further stabilisation.

ADVANTAGE - Any antigen or antibody can be fixed stably on the carriers. Stable and qualified carriers used in enzyme **immunoassay** can be prep'd. on a large scale. By using the carriers, enzyme **immunoassay** (EIA) can be made accurately with reduced error.

(J61186857-A)

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 ACCESSION NUMBER: 1986-172184 [27] WPIX
 CROSS REFERENCE: 1995-390286 [50]
 DOC. NO. NON-CPI: N1986-128520
 DOC. NO. CPI: C1986-073971
 TITLE: Immune body-adsorbent prepn. - by reducing sulphur-sulphur bond in antibody then crosslinking with binding gp of carrier.
 DERWENT CLASS: A96 B04 D16 S03
 PATENT ASSIGNEE(S): (ORIY) ORIENTAL YEAST CO LTD
 COUNTRY COUNT: 1
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 61103838	A	19860522	(198627)*		8
JP 07053759	B2	19950607	(199527)		4

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 61103838	A	JP 1984-225938	19841029
JP 07053759	B2	JP 1984-225938	19841029

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 07053759	B2 Based on	JP 61103838

PRIORITY APPLN. INFO: JP 1984-225938 19841029

AN 1986-172184 [27] WPIX

CR 1995-390286 [50]

AB JP 61103838 A UPAB: 19951221

S-S bond in the hinge part of an antibody is reduced, and the SH gp. in the resulting SH-contg. antibody is crosslinked with a binding gp. of a carrier to obtain an immune body-adsorbent.

The SH-contg. antibody is crosslinked with the SH gp. in the SH-contg. carrier in the presence of a cpd. having two or more maleimido gps. in one molecule. Alternatively SH-contg. antibody is crosslinked with the binding gp. in a carrier contg. one or more binding gps. of amino., imino, hydrazino, and prim. to **tert. amine** in the presence of a cpd. having both maleimido group and succinimido -ester gp. in one molecule.

Carriers are polysaccharides (agarose, sepharose, dextran, cellulose), synthetic resins (polystyrene, polyacrylamide, biogel, polyvinyl), glass or silica, kaolin, carbon, bentonite, yarn, wood, microorganisms, red blood cells of animals.

USE/ADVANTAGE - The antigen-bindability is high. Used as a carrier in **immunoaffinity chromatography**, a solid phase in **enzyme-immunoassay**, **immuno-sensor**, a **latex** in **latex-agglutination reaction**, etc.

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